

NON-FINAL ACTION

Applicant's amendment of 2-11-08 has been fully considered. The amended claims have overcome the previous rejections of 112/1st paragraph by correcting variable Z, and deleting "and prodrugs thereof" from claim 38. Thus, said rejections are withdrawn herein. However, new issues of 112 and 102 are noted, and thus new grounds of rejection is presented below.

Claims 1-34 and 42 are cancelled.

Claims 35-41 and 43 are pending.

In light of the new ground of rejection, the previous finality is now withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 35-41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 35 and 39 recite the term "solvate" which does not have a definition in the disclosure. Thus, it is unclear as to what solvents would be suitable for making a "solvate".

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 35-41 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using substituted pyrrolopyridine compounds, and a salt, N-oxide, and hydrate thereof does not reasonably provide enablement for making and using their **solvents**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 35 and 39 recite the limitation of “solvent” of compounds represented by formula (I). The term “solvent” covers various forms of the same

compound at different proportions of solvents. Thus, the scopes of claims 35 and 39 are unduly broad.

Claims 36-38, 40, 41 and 43 depend on claim 35 or 39, and thus, carry out the same broad scope of “solvate”.

The amount of direction or guidance presented: Although the specification lists possible salts and mentions “hydrates”, it does not describe “solvate” or provides guidance on what proportion of solvents to use for obtaining a “solvate”. Thus, the specification fails to provide sufficient enablement for making a “solvate” of the claimed compounds.

The state of the prior art: Although it is not unusual to expect a “solvate” of a compound, the process for selecting a solvent to make a solvate is not standard for all drugs since not all solvents can form solvates with all compounds. For the claimed compound, there is no reference teaching any possible solvate. Furthermore, the teaching of Vippagunta flatly states on page 18, section 3.4 the following:

“Predicting the formation of solvates or hydrates of a compound...is complex and difficult.”

Thus, the state of the prior art does not support the broad scopes of claims 35, 39 and claims dependent thereon.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select a “solvate” for each compound from the large Markush group of formula (I). Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50} , therapeutic index and active metabolites for each

“solvate”. Given a large Markush group of formula(I), such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a “solvate” is quite unpredictable because it is not possible to predict whether solid solutions will form and at what stoichiometry proportion (i.e, one, two, or half a molecule of solvent added per molecule of host) – see the following excerpt:

Each solid compound responds uniquely to the possible formation of solvates...and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent;...There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of ...solvates.

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make the hundreds of thousands of compounds and “solvates” of compounds represented by formula (I) recited in the above claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 35-41 and 43 are rejected under 35 U.S.C. 102(a) as being anticipated by **Choi-Sledeski et. al.** (WO 98/25611 – different inventive entity). The reference is relied on for the publication date of 6-18-98 which antedates the priority date of 6-3-99 which is the filing date of 09/090,492. Note, the earliest PCT is not published, and the first provisional application is currently not available. Thus, the earliest effective filing date cannot be ascertained.

On page 104, the first compound reads on the instant pyrrolopyridine formula with the following substituents:

- i. One of A₁, A₂ and A₃ is N while the other two are CH;
- ii. X₁, X_{1a}, X₃ and X₄ are all hydrogen atoms;
- iii. R₁ is hydrogen;
- iv. R₂ is R₃S(O)_p- wherein p = 2;
- v. R₃ is a heteroaryl group.

The disclosed compound can inhibit Factor Xa which exerts anticoagulant effect. It can also be administered with other agents as recited in claims 36-41 (see page 90, lines 25-36).

Claim Objections

4. Claims 35 and 39 are also objected to because of the following informalities: In the definition of X₃, choices are listed out of sequence (e.g., there is no items (a) and (d)) .

Appropriate correction is required.

Art Unit: 1624

On 4-8-08A telephone interview was conducted with Mr. Peter Mlynek regarding the above new grounds of rejection, and the withdrawn of finality.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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